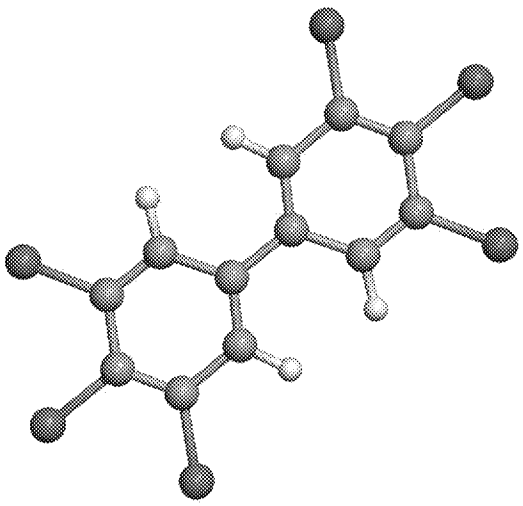


Mid-stream

Project Overview:

IRIS Assessment of PCBs (Non-Cancer Effects)

1-23-2017

PCB Team Meeting

Dave Bush
Joanne Trgovcich

ICF

Meeting Overview

- Review the PCB Assessment Process
- Review the Roles for EPA, ICF and Expert Authors
- Review Timeline for 2017
- Q&A

How does EPA conduct an "IRIS Assessment"?

NCEA carries out the assessment consistent with:

IRIS Handbook (June 2016)

- Still in draft form; still being revised

EPA Guidelines

- Cancer, developmental toxicity, etc.

2013 "IRIS Enhancements"

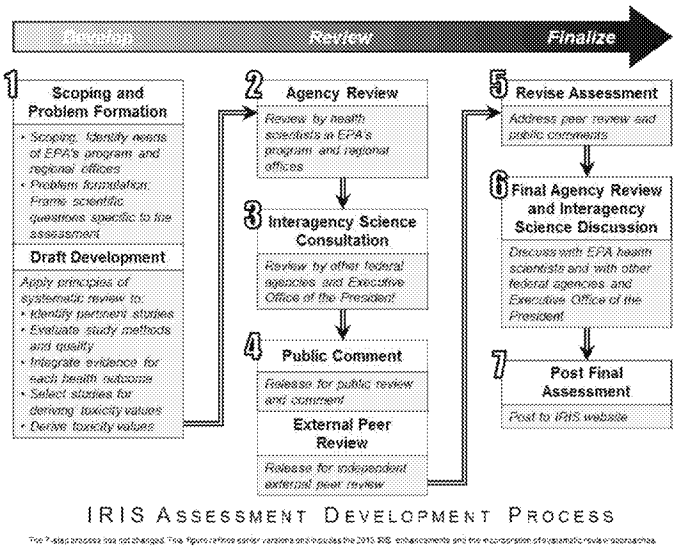
- More public input
- Employ principles of… **SYSTEMATIC REVIEW**
  - Transparency, consistency, replicability, continuous improvement
  - Incorporates recommendations from review of IRIS process by the National Research Council

How does EPA get there?

1. **Develop draft assessment**
2. **Review, review, review**
3. **Post final assessment**

Expert Authors will assist EPA with Step 1 - development of draft assessment (Toxicological Review)

And will ideally continue through assessment posting

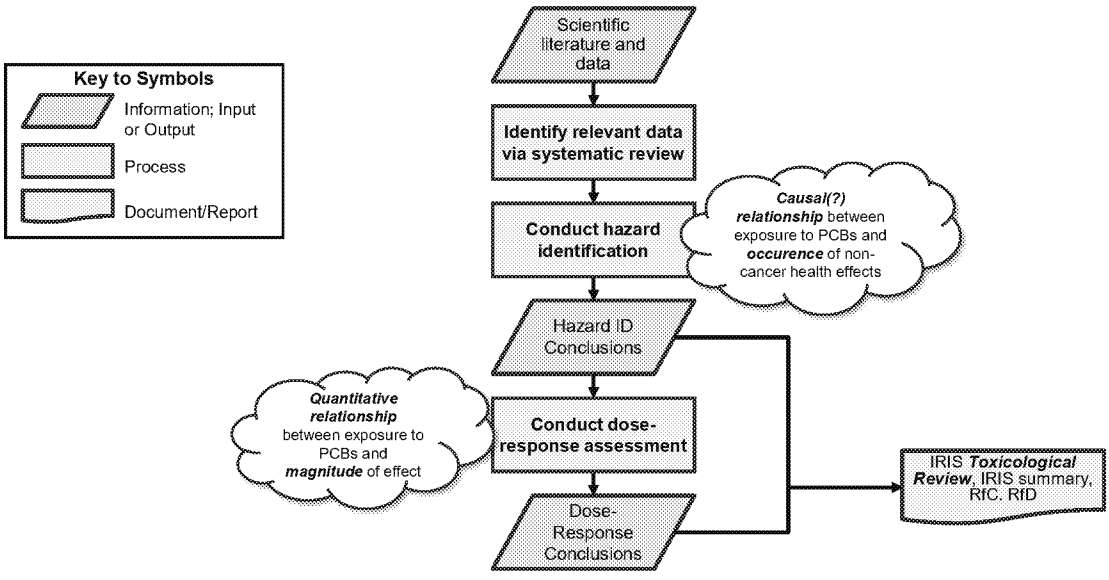


IRIS Assessment Development Process

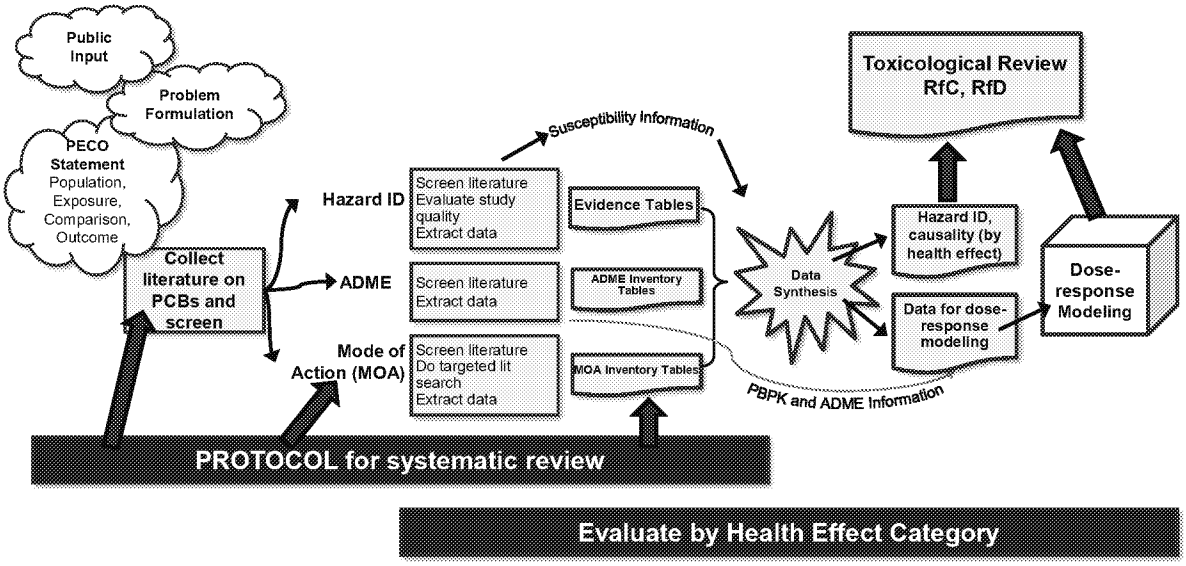
The 7-step process was not changed. This figure reflects earlier versions and includes the 2018 IRIS enhancements and the incorporation of systematic review approaches.

So how does the assessment happen???

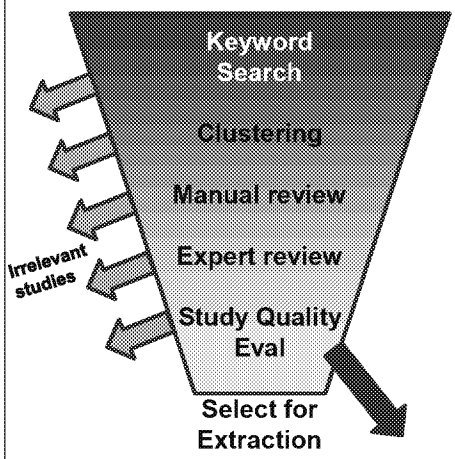
Developing the Toxicological Review
(simplified version)



Developing the Toxicological Review (more details)



Systematic Review (hazard identification)
Also relevant to MOA, ADME, susceptibility (with modifications)



Characteristics	Who?	How?
Very broad; 50,000+ studies	EPA	Traditional database search
Machine learning/clustering; results in categories based on relevance ("tiers")	ICF	DoCTER (ML algorithms developed by ICF)
Title/abstract screen; 2 independent reviewers, plus tertiary reviewer	ICF	DRAGON, screening protocol
"Analysis plan"; evaluated in light of PECO statement; scientific judgment	EPA, Authors (ICF support)	Free-form (Excel)
Study quality evaluation	EPA, ICF, Authors	DRAGON
Additional scientific judgment??	Experts, EPA	DRAGON

EPA Objective

Objective:

- Conduct IRIS assessment of PCBs (non-cancer effects ***only***)

Outcome: IRIS Toxicological Review of non-cancer effects of PCBs

- Hazard identification
- Dose-response assessment
  - Reference concentration (RfC)
  - (Oral) Reference dose (RfD)

Utility:

- Inform and establish science policy, develop regulations, set clean-up goals

Focus:

- Risk resulting from exposure to complex mixtures of PCB congeners

ICF Role

Provide technical support in developing the Toxicological Review across all aspects of scientific assessment

- Literature search and screening
- Identify, recruit and provide support to non-EPA expert authors
- Provide support for study quality evaluation, data extraction and synthesis of draft

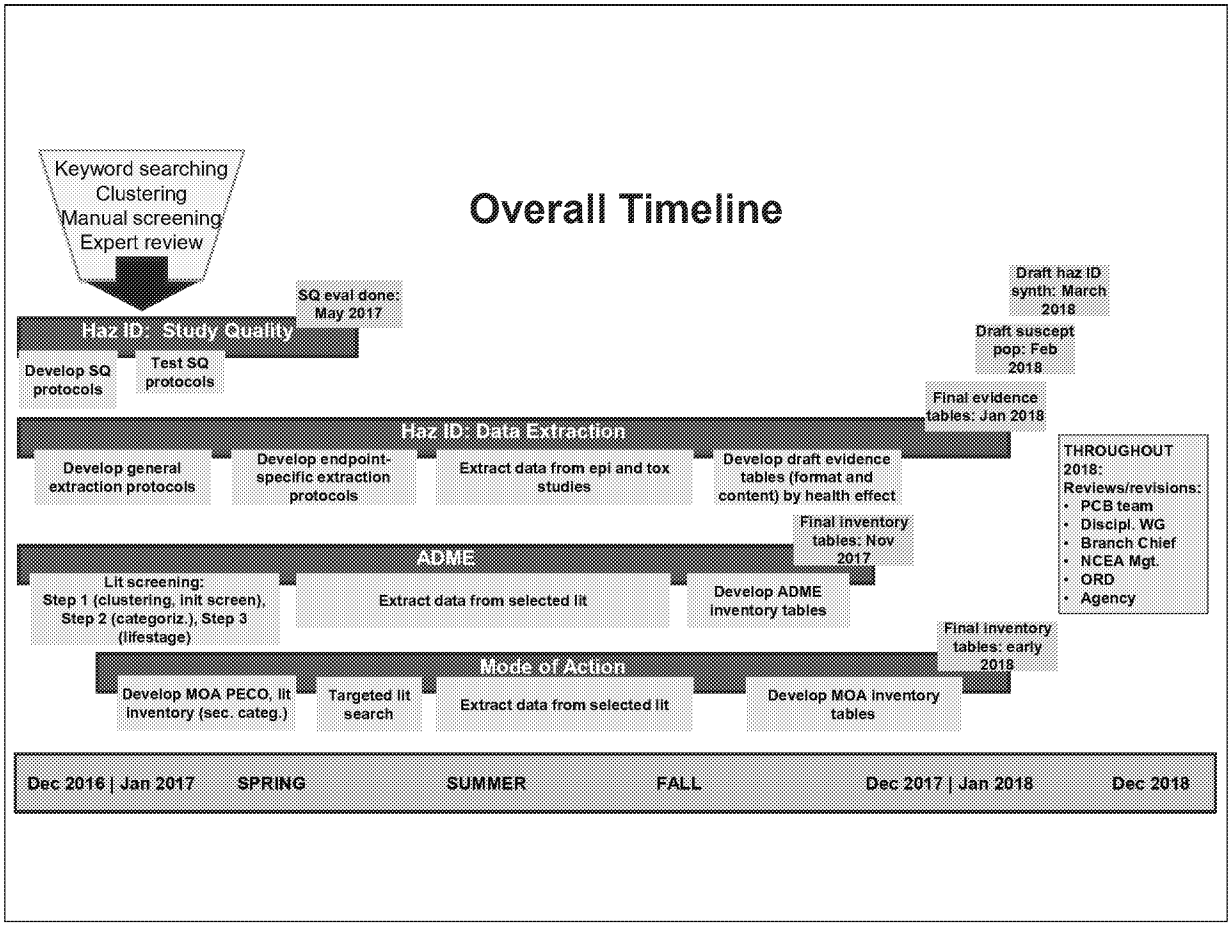
Expert Author Roles

Provide specific expertise in developing the Toxicological Review for your health effect(s)

- Communicate with PCB team through teleconferences
- Finalize preliminary analysis plans and literature inventories
- Contribute to development and implementation of study quality evaluation protocols
- Develop data extraction protocol
- Identify studies providing dose-response data
- Develop PECO statements for MOA studies
- Review studies relevant to biological considerations for dose-response analysis
- Draft the health effect category synthesis section
- Draft mode-of-action summaries

EPA and Expert Author Section Leads

PCB Health Effects Lead Authors				
Health Effect	Toxicologist		Epidemiologist	
	Lead Author	Affiliation	Lead Author	Affiliation
Cardiovascular	Michal Toborek	University of Miami	Alexander Sergeev	Ohio University
Dermal and Ocular	Marian Rutigliano	EPA	Marian Rutigliano	EPA
Developmental	Aileen Keating	Iowa State University	John Meeker	University of Michigan
Endocrine	April Luke	EPA	Michael Bloom	University at Albany SUNY
Gastrointestinal	April Luke	EPA	EPA	EPA
Hematological	MaryJane Selgrade	ICF	EPA	EPA
Hepatic	Larry Robertson	University of Iowa	EPA	EPA
Immunological	MaryJane Selgrade	ICF	Todd Jusko	University of Rochester
Metabolic	Marian Rutigliano	EPA	Marian Rutigliano	EPA
Neurological	Pamela Lein	UC Davis	Sharon Sagiv	UC Berkeley
Reproductive	Aileen Keating Xabier Arzuaga Erin Yost	Iowa State University EPA EPA	Pam Factor-Litvak	Columbia University


Overall Timeline
Keyword searching
Clustering
Manual screening
Expert review
SQ eval done: May 2017
Haz ID: Study Quality
Develop SQ protocols
Test SQ protocols
Draft haz ID synth: March 2018
Draft suscept pop: Feb 2018
Final evidence tables: Jan 2018
Haz ID: Data Extraction
Develop general extraction protocols
Develop endpoint-specific extraction protocols
Extract data from epi and tox studies
Develop draft evidence tables (format and content) by health effect
THROUGHOUT 2018:
Reviews/revisions:
• PCB team
• Discipl. WG
• Branch Chief
• NCEA Mgt.
• ORD
• Agency
Final inventory tables: Nov 2017
ADME
Lit screening:
Step 1 (clustering, init screen), Step 2 (categoriz.), Step 3 (lifestage)
Extract data from selected lit
Develop ADME inventory tables
Final inventory tables: early 2018
Mode of Action
Develop MOA PECO, lit inventory (sec. categ.)
Targeted lit search
Extract data from selected lit
Develop MOA inventory tables
Dec 2016 | Jan 2017
SPRING
SUMMER
FALL
Dec 2017 | Jan 2018
Dec 2018

Upcoming Tasks for Authors

- **Final updates for hazard ID literature**
  - Includes group of peer-reviewed literature incorrectly listed as not peer-reviewed early in the process
  - Includes updates for redirected IDs and some tag changes reflecting studies for which PDFs became available between the last report (10/17/16) and this report
  - Will allow authors to finalize their inventory tables (inventories due 60 days after receiving final update)
- **MOA literature review**
  - In conjunction with hazard ID studies that inform MOA, will be used to develop a keyword list that we will use for more focused literature searches and screens
  - Authors will identify likely mechanisms, and develop PECO statements for each mechanism relevant to their health effect
- **Identify studies relevant to biological considerations for dose-response analysis**
  - Authors will identify studies and specific datasets that inform exposure risks to the general population, susceptible populations, and from exposure during particular periods of development
- **Study quality evaluation**
  - Authors will contribute to developing/finalizing SQ protocols and implement protocols
  - Quality and other criteria will be used to prioritize studies that will be the focus of the draft synthesis and evidence tables

Upcoming Team Meetings

Date	Topic
2/6/2017	No Meeting
2/13/2017	MOA check-in - MOA literature inventories
2/27/2017	HERO training- LitCiter orientation

Q&A

Mid-stream
Project Overview:

IRIS Assessment of PCBs (Non-Cancer Effects)